The Wound Healing Process: Inflammation

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INFLAMMATION ETIOLOGY

The onset of a wound starts a cascading effect inducing the inflammatory response. The activator of the **inflammation** response appears to originate fr diapedesis of free circulating phagocytes due to the release of endotoxin of th damaged cells. The process appears to begin by the migration of phagocytes between the endothelial cells, thus triggering Leukotrienes for the Hageman cascade. The Hageman cascade begins the production of bradykinin a vasodilator, through the Fletcher Factor, which induces the enzyme kallikrein precursor for production of the bradykinin. Along with the production of the kinins in the Hageman Cascade, prothrombin is converted to thrombin, a lysin enzyme for the blood platelets and activating agent for fibrinogen. The fibrinogen in the plasma breaks down and develops a fibrin meshwork for the blood platelets to adhere to at the wound site. The blood platelets then begin lysing action by the thrombin, thus inducing the release of the platelet factors The platelet release factors consist of growth factors and coagulation mediato for fibroblast. During this **inflammation** phase there are many factors that m arrest the wounds healing ability and leave it in stasis at this stage. Perhaps th greatest causative agent for chronic **inflammation** is infection. The infection wound may not be as easy to spot as one may think. There are circumstances when a wound may develop sinus tracts to which the infection may migrate away from the wound, thus appearing to show no reason for the **inflammati** This type of problem may lead to a negative C & S result, only to have the infection reoccur with full force at a later time. The health care practitioner should examine the wound along the edges after a debridement for possible s

tracts if the wound appears to remain in a chronic **inflammation** stage.

Diabetic neuropathy may pose a problem with the **inflammation** process b desensitizing the neurons. Should the neurons become unable to function the pain portion of the **inflammation** process will be diminished, thus leading to possible compound problems. One of the problems associated with **diabetic neuropathy** is Charcot's Joint. In a **diabetic** patient examination of the feet i important for the potential development of Charcot's joint. The examination should include looking for **inflammation** and the possible development of th late stage "rocker bottom" of the foot. Chronic **inflammation** may also be a of an underlying granuloma or multiple granulomas. The practitioner should examine the surrounding tissue of the wound for possible development of granulomas under the new epidermal tissue growth.

Another problem not often looked into is the absence of **inflammation**. As o can see **inflammation** plays a key role in the healing process, but many facto can suppress this action. The most notable factor affecting the **inflammation** process is low blood supply to the wound site. Without the proper blood sup hemostasis will be slower and the chemotactics will be slow to produce the needed chemotaxis for the phagocytes to be directed to the wound. The bloo flow around a wound can be evaluated by testing the $TCPO_2$ (Trans-Cutaneo Pressure) around the wound site. A low reading of the $TCPO_2$ (<30 mm) ma indicate localized or systemic circulatory problem, thus leading to the reducti of the inflammatory factors. Another problem associated with the absence of **inflammation** is a pharmaceutical induced suppression of the **inflammation** One of the most common prescribed pharmaceuticals that produces this effec the steroids, most notably glucocorticoids and mineralcorticoids. These stero are believed to suppress the inflammatory mediators directly by affecting the arachidonic acid metabolism; thus reducing the thromboxane, prostaglandin's and prostacyclin enzymes needed for the **inflammation** cascade. The health c practitioner should access the patient for possible wounds or ulcers prior to administration of these steroids, thus avoiding a potential chronic wound condition. In general, if the wound remains or fails to enter the **inflammation** process one should investigate the possible etiology for a causative agent or underlying problem.

DIAGNOSTICS OF CHRONIC WOUND INFLAMMATION

Most chronic wounds can be avoided by the early detection of the etiology. T **inflammation** process is the best visual sign for the practitioner to start with but there are other diagnostic test to pinpoint the problem. The practitioner should develop a rigid series of steps in the differentiation and diagnostics, an apply this series to all patients showing signs of potential wound or ulceration development. The first step is the physical examination of the site, this should include palpation for abnormalities and light debridement to allow visibility if wound is open, also if feasible a Doppler test should be performed to determi the state of the arterial blood flow in the lower extremities. If the examination

includes the foot a monofilament test should be performed to check for possi **neuropathy**, pressure should be applied to the point of the monofilament bending,. While completing the physical examination one can differentiate the probability of cellulitis or other diseases from circulatory problems by the Dependent Rubor Test, this is accomplished by elevating the legs and observi the color change of the foot. The next step is to rule out the possibility of infection. This step can be accomplished through a culture and sensitivity test the wound is open or aspiration of a closed site if underlying infection is suspected.

Also, a roentgenograph should be performed to rule out Osteomyelitis; the practitioner should not wait until the bone is exposed in an open wound to lo for Osteo. Next, one should perform a series of blood test, CBC with differen and glucose test to rule out diabetes. If a patient is known to have, or is diagnosed with diabetes a Glycosylated Hemoglobin test should be performed The values of the Glycosylated Hemoglobin test vary, but in general the norm are measured in percentages with, Hbs_{1a} 1.6%, Hbs_{1b} 0.8%, HbA_{1c} 5%, and total range is 5.5% to 9%. The Glycosylated Hemoglobin test can give the lo term picture of the diabetes control. The diagnostic and differentiation procedures should be developed by the practitioner to suit their patients need but a standard of sequence is highly recommend.

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(Beeson, McDermott, Wyngaarden, 1979) Cecil Textbook of Medicine (15th ed). Philadelphia: W. B. Saunders Co.

(Loeb et al., 1994) Illustrated Guide to Diagnostic Test. Pennsylvania: Springhouse.

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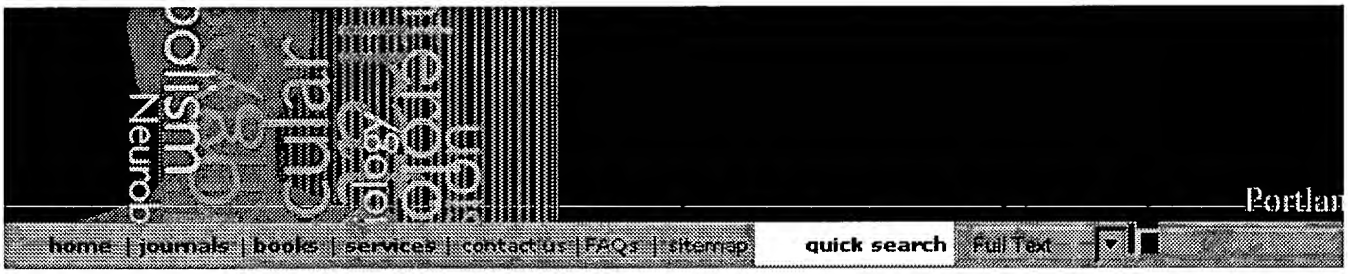

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Skin microcirculation in patients with Type 1 diabetes with and without neuropathy after neurovascular stimulation

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Key words: diabetic neuropathy, Type 1 diabetes, neurogenic inflammation, nutritive capillary blood flow, total skin blood flow.

Abbreviations: CBV, capillary blood cell velocity; LDF, laser Doppler flux.

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1. Neurovascular inflammation is impaired in patients suffering from diabetic neuropathy. The aim of our study was to evaluate the distribution of nutritive and total skin blood flow in diabetic patients with and without neuropathy after neurovascular stimulation with acetylcholine.

2. Twenty patients with Type I diabetes, 10 with and 10 without neuropathy, and 10 age-matched non-diabetic control subjects, underwent microvascular investigations before and after neurovascular stimulation by intracutaneous application of acetylcholine. The capillary blood cell velocity in the nailfold of the hallux was measured by videophotometric capillaroscopy, and the total skin microcirculation in the same area by laser Doppler flowmetry.

3. The increase in total skin blood flow was significantly impaired in the group of neuropathic diabetic patients compared with the non-neuropathic diabetic patients (17.5 ± 8.3 versus 51.0 ± 16.2; $P < 0.05$) and the non-diabetic subjects (17.5 ± 8.3 versus 67.8 ± 19.7; $P < 0.01$). The increase in capillary blood flow was not significantly impaired in Type I diabetes patients with neuropathy.

4. The ratio between capillary blood flow and total skin perfusion decreased significantly in the control group (from 0.82 ± 0.15 to 0.47 ± 0.11; $P < 0.005$) and in the Type I diabetes patients without neuropathy (from 0.79 ± 0.12 to 0.43 ± 0.12; $P < 0.05$), whereas the decrease in the neuropathic group was statistically insignificant (from 1.05 ± 0.19 to 0.72 ± 0.16).

5. Diminished total skin perfusion in the foot after intracutaneous stimulation with acetylcholine in Type I diabetes patients is associated with diabetic neuropathy, indicating a disturbance in the neurovascular reflex

diabetes patients is associated with diabetic neuropathy, indicating a disturbance in the neurovascular reflex arc. This impaired neurovascular response is caused by a diminished total and subpapillary blood flow and not by a diminished nutritive capillary flow. There is no evidence of a diminished nutritive capillary blood flow during neurogenic inflammation in Type I diabetes patients suffering from diabetic neuropathy.

L3 ANSWER 30 OF 30 MEDLINE
ACCESSION NUMBER: 87325279 MEDLINE
DOCUMENT NUMBER: 87325279 PubMed ID: 3115210
TITLE: Efficacy and safety of nonsteroidal **anti-inflammatory** drugs in the therapy of diabetic neuropathy.
AUTHOR: Cohen K L; Harris S
SOURCE: ARCHIVES OF INTERNAL MEDICINE, (1987 Aug) 147 (8) 1442-4. Journal code: 0372440. ISSN: 0003-9926.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198710
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19871013

AB A study comparing ibuprofen (600 mg four times a day) vs sulindac (200 mg twice a day), and a placebo in the treatment of painful diabetic peripheral neuropathy was conducted in 18 male outpatients. Discomfort was characterized and rated with a subjective neuropathy score. The response to both ibuprofen and sulindac was better than it was to placebo in the entire group. There were no changes in glucose control or renal function. Further studies are necessary to evaluate the significance of aldose reductase-inhibitor properties of nonsteroidal **anti-inflammatory** drugs and to select the "best" one of these drugs for the treatment of diabetic neuropathy.

L3 ANSWER 22 OF 30 MEDLINE
ACCESSION NUMBER: 95094099 MEDLINE
DOCUMENT NUMBER: 95094099 PubMed ID: 8000974
TITLE: The influence of sulindac on experimental streptozotocin-induced diabetic neuropathy.
AUTHOR: Zochodne D W; Ho L T
CORPORATE SOURCE: Department of Clinical Neurosciences, University of Calgary, Alberta, Canada.
SOURCE: CANADIAN JOURNAL OF NEUROLOGICAL SCIENCES, (1994 Aug) 21 (3) 194-202.
Journal code: 0415227. ISSN: 0317-1671.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 19950215
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AB We studied the influence of sulindac, a nonsteroidal **anti-inflammatory** agent on experimental streptozotocin-induced diabetic neuropathy. Untreated diabetic rats were compared with nondiabetic rats, diabetic rats treated with low dose insulin and diabetic rats given sulindac (6.0 mg/kg by gavage 5 of 7 days weekly). Neuropathy was assessed by following serial in vivo motor and sensory caudal conduction, resistance to ischemic conduction failure, and in vitro conduction in sural myelinated and unmyelinated sensory fibers. The impact of low dose insulin and sulindac treatment on the microenvironment of the L4 dorsal root ganglion and sciatic endoneurium was assessed by measuring local perfusion and oxygen tension after 16 weeks of diabetes. Sulindac normalized conduction velocity in caudal sensory fibers, sural myelinated fibers and sural unmyelinated fibers, and reduced the number of diabetic cataracts. Sulindac also normalized a deficit in dorsal root ganglion blood flow and a reduction in sciatic endoneurial oxygen tension in diabetic rats. Low dose insulin improved neuropathy as well but the pattern of benefits was less robust than that of sulindac. Sulindac may be a candidate for a clinical trial in human diabetic polyneuropathy.

L Number	Hits	Search Text	DB	Time stamp
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2	0	lacuna adj2 aminobicyclic	USPAT; US-PGPUB	2003/06/06 12:24
3	0	lacuna adj diabetic	USPAT; US-PGPUB	2003/06/06 13:10
4	0	lacuna adj2 neuropathy	USPAT; US-PGPUB	2003/06/06 13:52
5	26707	diabetes	USPAT; US-PGPUB	2003/06/06 13:52
6	1483	diabetic adj neuropathy	USPAT; US-PGPUB	2003/06/06 14:04
7	964	diabetes and (diabetic adj neuropathy)	USPAT; US-PGPUB	2003/06/06 13:52
8	0	(diabetes and (diabetic adj neuropathy)) and benzylidenesuccinic	USPAT; US-PGPUB	2003/06/06 13:52
9	120	(diabetes and (diabetic adj neuropathy)) and (succinic adj acid)	USPAT; US-PGPUB	2003/06/06 13:53
10	224	(diabetic adj neuropathy) and antiinflammatory	USPAT; US-PGPUB	2003/06/06 14:21
11	2252	treating adj inflammation	USPAT; US-PGPUB	2003/06/06 14:21
12	8	(treating adj inflammation) and (diabetic adj neuropathy)	USPAT; US-PGPUB	2003/06/06 14:22